UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

IN RE: FRESENIUS GRANUFLO/NATURALYTE DIALYSATE PRODUCTS LIABILITY LITIGATION

MDL No. 1:13-MD-2428-DPW

REDACTED FILING

LEAVE TO FILE GRANTED ON SEPTEMBER 8, 2017

This Document Relates to:

Mervin Boyd, Individually and as Wrongful Death Beneficiary of Judith Boyd, Case No. 1:13-cv-11717-DPW;

Charles Cameron, Individually and as Wrongful Death Beneficiary of Charles Cameron, Sr., Case No. 1:13-cv-12446-DPW;

Daniel Carter, Individually and on Behalf of the Wrongful Death Beneficiaries of Anniece Carter, Case No. 1:13-cv-12459-DPW;

Joyce Marie Clark, Individually and on Behalf of the Wrongful Death Beneficiaries of Edward Lee Jenkins, Case No. 1:13-cv-12460-DPW;

Kathy Dennis as Wrongful Death Beneficiary of Ruth Ann Dennis, Case No. 1:13-cv-12467-DPW;

Geraldine Dillingham, as Next of Kin and Personal Representative of Estate of Ronnie Dillingham, Case No. 1:15-cv-12796-DPW;

Gloria Cothern Dunaway, Individually and as Wrongful Death Beneficiary of Betty Sue Cothern, Case No. 1:13-cv-11714-DPW;

Carlotta Jerry, Individually and as Next of Kin of Christopher Jerry, Case No. 1:15-cv-14121-DPW;

Alex Kazos, as Next of Kin and Personal Representative of Estate of Nick Kazos,

Case No. 1:15-cv-12376-DPW;)
)
Janice McGhee, Individually and as Wrongful)
Death Beneficiary of Henry McGhee,)
Case No. 1:13-cv-13172-DPW;)
)
Michael McNulty, Individually and as Wrongful)
Death Beneficiary of Willie Enette McNulty,)
Case No. 1:13-cv-12403-DPW;)
)
Sharon Randall, as Next of Kin and Personal)
Representative of Estate of Winfitch Randall,)
Case No. 1:15-cv-12735-DPW;)
)
Amy Riben, Wife, and Max Riben, Husband,)
And Their Marital Community,)
Case No. 1:15-cv-11134-DPW;)
)
Kimberly Ross, Individually and on Behalf of the)
Wrongful Death Beneficiaries of Stella Ross,)
Case No. 1:13-cv-12478-DPW;)
)
Sophia Walker, Individually and on Behalf of the)
Wrongful Death Beneficiaries of Hattie Myles,)
Case No. 1:13-cv-12487-DPW;)
)
Beulah Williams, on Behalf of the Wrongful)
Death Beneficiaries of Angela Hughes,)
Case No. 1:13-cv-12486-DPW)
_____)

STATEMENT OF UNDISPUTED MATERIAL FACTS IN SUPPORT OF FMCNA'S MOTION FOR SUMMARY JUDGMENT ON THE CLAIMS OF OPT-OUT PLAINTIFFS THAT ARE BARRED BY THE LEARNED INTERMEDIARY DOCTRINE

Pursuant to Federal Rule of Civil Procedure 56, Defendants, Fresenius Medical Care Holdings, Inc., Fresenius USA, Inc., Fresenius USA Manufacturing, Inc., and Fresenius USA Marketing, Inc. (collectively "FMCNA") submit this statement of undisputed material facts in support of their motion for summary judgment on the claims of all opt-out plaintiffs who received their relevant dialysis treatments preceding their alleged injury: (1) at an FMCNA dialysis unit at any time; (2) at a DaVita dialysis unit after November 4, 2011; or (3) at any dialysis unit after March 29, 2012. The plaintiffs whom FMCNA has currently identified who are subject to this motion include: Mervin Boyd (Judith Boyd); Charles Cameron (Charles Cameron, Sr.); Daniel Carter (Anniece Carter); Joyce Marie Clark (Edward Lee Jenkins); Kathy Dennis (Ruth Ann Dennis); Geraldine Dillingham (Ronnie Dillingham); Gloria Cothern Dunaway (Betty Sue Cothern); Carlotta Jerry (Christopher Jerry); Alex Kazos (Nick Kazos); Janice McGhee (Henry McGhee); Michael McNulty (Willie Enette McNulty); Sharon Randall (Winfitch Randall); Max Riben (Amy Riben); Kimberly Ross (Stella Ross); Sophia Walker (Hattie Myles); and Beulah Williams (Angela Hughes).

Facts Applicable to All Plaintiffs

1. FMCNA's Chief Medical Office issued several memoranda between 2000 and 2011 that relate to issues such as GranuFlo® and NaturaLyte®, acetate, acid-base balance, serum bicarbonate levels, alkalosis, the concept of "total buffer," and potential mortality and cardiac risks. Ex. 1 (December 7, 2000 Memo); Ex. 2 (March 23, 2001 Memo); Ex. 3 (Apr. 5, 2002 Memo); Ex. 4 (July 5, 2005 Memo); Ex. 5 (Oct. 30, 2008 Email and Memo); Ex. 6 (Apr. 13, 2009 Email and Memo); Ex. 7 (Aug. 27, 2009 Email, Memo and Spreadsheet Excerpt); Ex. 8 (Nov. 4, 2011 Email and Memo).

2. FMCNA's Chief Medical Office memorandum dated December 7, 2000, was addressed to FMC Medical Directors regarding the subject of "Bicarbonate Dialysate and Low Serum Bicarbonate Levels." Ex. 1.

3. The December 7, 2000, memorandum included data regarding the distribution of pre-dialysis serum bicarbonate levels in FMCNA facilities and data regarding the distribution of dialysate bicarbonate prescribed in all patients' most recent hemodialysis order in FMCNA facilities. Ex. 1, p. 2-6, 8.

4. The December 7, 2000, memorandum provided, in part, that "it appears that one must order a total dialysate buffer of 38 to 40 mmol/l to obtain a mean facility serum bicarbonate level of 22 mmol/l," and included the following table illustrating "the total dialysate buffer obtained from various dialysate series with different dialysis machine bicarbonate settings." Ex. 1, p. 6-7.

Table II

Examples to Obtain Indicated Total Buffer										
9000 Series (Liquid)		9000 Series GranuFlo		6000 Series GranuFlo		6000 Series (Liquid)		4000 Series (Liquid)		
Bicarb Setting	Acetate	Bicarb Setting	Acetate	Bicarb Setting	Acetate	Bicarb Setting	Acetate	Bicarb Setting	Acetate	Total Buffer
39	4	35	8	37	6	40	3	39	4	43
36	4	32	8	34	6	37	3	36	4	40
34	4	30	8	32	6	35	3	34	4	38
32	4	28	8	30	6	33	3	32	4	36

5. The December 7, 2000, memorandum provided, in part, "You must consider that the buffer activity from acetate in the acid solution contributes to the total buffer – particularly in the GranuFlo dialysate." Id. at p. 7. It further provided, in part, "Because of the increased

acetate in the acid portion of GranuFlo powder (which is metabolized to bicarbonate), significantly higher base is delivered." Id. at p. 8.

6. The December 7, 2000, memorandum further provided, in part:

> I urge you to review each individual patients' bicarbonate levels in your facility and your overall facility distribution…. It appears that, except in the case of GranuFlo, the dialysis machine bicarbonate settings should be 35 mmol/l or higher since below that prescription, very low serum bicarbonate levels occur in a high percentage of patients. Depending on the concentrate type, it may be necessary to set the machine dialysate bicarbonate as high as 40 mmol/l for some patients. In patients who have normal to high pre-dialysis levels, or in whom you have concern for the affects of high post-dialysis levels which may be adversely affect a co-morbid condition, individual dialysate bicarbonate levels should be prescribed….

Id. at p. 9.

7. The December 7, 2000, memorandum attached 4 reference articles on acid-base balance and was posted on the FMCNA Intranet. Id. at p. 9-43.

8. FMCNA's Chief Medical Office memorandum dated March 23, 2001, was addressed to FMC Medical Directors, DoNs, and Administrators regarding the subject of "Delivered Bicarbonate and Total Buffer with Fresenius 2008H and 2008K Dialysis Machines." Ex. 2.

9. The March 23, 2001, memorandum provided, in part:

> [A]t the patient level, the sodium acetate concentration is added to this bicarbonate level to determine the total buffer which results. This is because acetate is metabolically converted to bicarbonate in the body.
>
> ….
>
> When Granuflo is used, an advantage accrues in that there is a greater amount of acetate available to be metabolically converted to bicarbonate in the body.

Ex. 2, p. 1-2.

10. The March 23, 2001, memorandum further provided, in part:

> Once dialysate contacts and interacts with the patient's blood, acetate is metabolically converted to bicarbonate. (Illustrated in the right side of Figures 1 and 2). Thus, the total buffer is the sum of the acetate and bicarbonate. Therefore, one must add the delivered acetate to the delivered bicarbonate to appreciate the total buffer which the patient is receiving.
>
> In summary:
>
> 1. The amount of bicarbonate delivered to the patient is determined by the bicarbonate setting on the dialysis delivery machine, not necessarily the bicarbonate concentration on the label.
>
> 2. Setting the bicarbonate level must be carried out prior to initiation of each dialysis….
>
> 3. The bicarbonate and acetate delivered must be added to determine the total buffer provided to the patient.
>
> 4. The physician and the facility staff must take the following steps prior to dialysis:
>
>   a. Select and provide an appropriate acid and bicarbonate concentrate.
>
>   b. Select (physician) and appropriately set (facility staff) the sodium and bicarbonate along with the potassium, calcium and magnesium to be delivered to each patient before each dialysis….
>
>   c. Observe and monitor the patient's serum bicarbonate level to determine that the prescribed dialysate bicarbonate is actually being delivered and is appropriate for that particular patient. If not, the physician should establish a new bicarbonate prescription and the staff should readjust the bicarbonate setting as is appropriate….
>
>   d. It is my recommendation that physicians review the 'Verify Concentrate' screen with the technical and nursing staff to witness how the bicarbonate level is altered by changing the potassium, calcium, and magnesium levels and vice versa….

Ex. 2, p. 3-4.

11. The March 23, 2001, memorandum further included attachments that noted that 9000 Series liquid acid concentrate contributes 4.0 acetate and 1000 Series GranuFlo contributes 8.0 acetate to the dialysate solution. Ex. 2, p. 6-7, 9-10.

12. FMCNA's Chief Medical Office memorandum dated April 5, 2002, was addressed to FMC Medical Directors regarding the subject of "Serum Bicarbonate Levels." Ex. 3.

13. The April 5, 2002, memorandum included graphs depicting the mean serum bicarbonate level for FMC facilities from February of 2001 through February of 2002 and provided, in part:

> In my previous memos on this subject, I suggested that bicarbonate therapy should be individualized…. I would like to reiterate that those patients who are acidotic – that is predialysis serum bicarbonate levels below 19 to 20 meq/L should appropriately receive higher bicarbonate dialysate. However, those patients who have predialysis serum bicarbonate levels above 28 to 30 meq/L and medical conditions which cause concern about post-dialysis alkalosis, should receive a lower dialysate bicarbonate concentration.... I would urge you to … order specific and appropriate levels of bicarbonate dialysate for each individual patient.

Ex. 3, p. 1.

14. FMCNA's Chief Medical Office memorandum dated July 5, 2005, was addressed to FMC Medical Directors regarding the subject of "Bicarbonate Levels." Ex. 4.

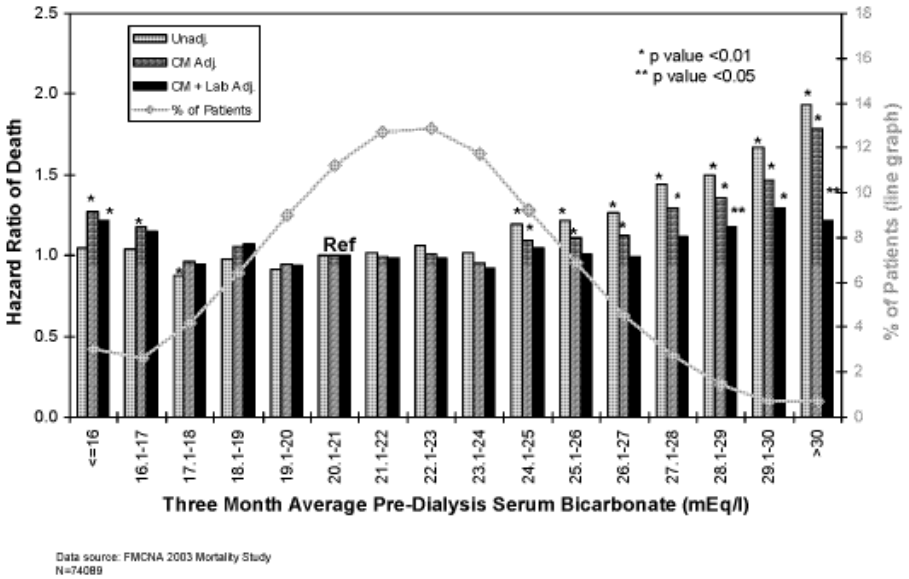
15. The July 5, 2002, memorandum provided, in part:

> Several years ago we initiated an effort to improve bicarbonate levels in patients in our dialysis facilities. At that time, I provided data indicating that the mean serum bicarbonate in the patient population was approximately 20 mmol/L with a number of patients below 18 mmol/L. A plan to educate staff and physicians was implemented regarding the manner by which the 2008H and 2008K machines deliver bicarbonate as well as our initiating use of GranuFlo (a dry bicarbonate delivery system). With these efforts, we have now increased the mean bicarbonate for FMCNA patients to approximately 24 mmol/L.

Ex. 4, p. 1.

16. The July 5, 2002, memorandum included the following figure that illustrates "a hazard risk analysis which identifies the risk of death at various levels of bicarbonate (unadjusted and with case mix and lab adjustment)." Ex. 4, p. 2.

Figure 3



17. The July 5, 2002, memorandum further provided, in part:

You will note from this death risk analysis that after adjustment for lab (nutrition), there is no statistically significant increase in death risk until patient bicarbonate pre-dialysis values are at or above 28 mmol/L…. This suggests that a level of pre-dialysis serum bicarbonate of up to 28 mmol/L would be acceptable…. [T]here is no increased hazard risk between 24 and 28 mmol/L of serum bicarbonate.

However, I believe we are at a point where we should consider modulating the increase in bicarbonate values. Examination of the distribution curve of bicarbonate values for the entire Company as well as individual dialysis facilities demonstrates the persistence of biologic distribution…. This suggests that bicarbonate therapy should be managed much like potassium – that is, the vast majority of patients may be appropriately treated with a common bicarbonate dialysate prescription but some patients will require lower bicarbonate dialysate while others may require a higher bicarbonate dialysate….

A final issue of which you should be aware is that GranuFlo derived dialysate delivers an additional 4 med/L of sodium acetate.... GranuFlo was developed as a completely 'dry' acid concentrate using Sodium Diacetate powder. Sodium Diacetate is a combination of Acetic Acid and Sodium Acetate; therefore the acetate concentration in GranuFlo is double that of traditional liquid acid concentrates.

> The acetate contributed from liquid acid concentrates or from GranuFlo to the final dialysate is metabolized by the patient, converting it to bicarbonate. Therefore, it is important to understand and prescribe a dialysate bicarbonate concentration which, in combination with the acetate in the acid concentrate, delivers the desired total buffer. We anticipate that for every 4 meq/L decrease or increase in the dialysate total buffer there will be a corresponding 1 – 2 meq/L change in the pre dialysis serum bicarbonate.

Ex. 4, p. 3.

18. The July 5, 2002, memorandum included a table with columns for potential bicarbonate prescriptions, the acetate contribution from GranuFlo (8 meq/L) and liquid acid (4 meq/L), and the resulting "total buffer." Ex. 4, p. 4.

19. To illustrate the concept of "total buffer," the July 5, 2002, memorandum also attached "four figures which represent face shots of the 2008 Delivery System," and stated, "one must add the acetate (left side and circled) to the bicarbonate content to obtain the total buffer." Ex. 4, p. 4-6.

20. The July 5, 2002, memorandum further provided, in part, "I believe this information about the current status of bicarbonate outcomes is important and may affect your dialysate prescription." Ex. 4, p. 6.

21. FMCNA's Chief Medical Office memorandum dated October 30, 2008, was addressed to FMS Medical Directors regarding the subject of "Dialysate Concentrate." Ex. 5.

22. The October 30, 2008, memorandum provided, in part:

> Renal Therapies Group (RTG)…. has made the decision to move entirely to the 4000 series. During this conversion, RTG will also make several other changes to dialysate concentrate…. Bicarbonate will be available in 35 mEq/L thru 40 mEq/L. As you are aware, the bicarbonate concentration can be varied as you desire using the 2008H and K delivery machines. Be mindful that changes in the bicarbonate concentration cause reciprocal changes in the potassium and calcium concentrations because of proportioning in the 2008H and K machines.

Ex. 5, p. 1-2.

23. The October 30, 2008, memorandum further attached a concentrate flashcard that noted that Naturalyte 4000 Series Acid Concentrate contributes 4.0 acetate and GranuFlo 2400 Series Dry Acid Concentrate contributes 8.0 acetate to the dialysate solution. Ex. 5, p. 4.

24. FMCNA's Chief Medical Office memorandum dated April 13, 2009, was addressed to FMS Medical Directors regarding the subject of "Dialysate Concentrate Change and Bicarbonate/Buffer." Ex. 6.

25. The April 13, 2009, memorandum provided, in part:

> The bicarbonate setting being delivered and displayed on the screens of the 2008 H & K delivery machines represents only the bicarbonate level in the dialysate. This number does **NOT** include the 4 meq/L of acetate delivered by the liquid acid solution or the 8 meq/L of acetate delivered by the Granuflo acid powder. Therefore, please keep in mind the following:
>
> - The 'default' setting of bicarbonate after switching to the 4000 series concentrate has been set at 33 meq/L of HCO_3.
> - If the facility uses liquid acid concentrate, there is an additional 4 meq/L of acetate which is quickly converted to bicarbonate.
>   - Therefore, the bicarbonate (or actually total buffer) provided to the patient when using liquid acid is 37 meq/L.
> - If the facility uses Granuflo (powder) there is an additional 8 meq/L of acetate, which is converted to bicarbonate.
>   - Therefore, the bicarbonate (or actually total buffer) provided to the patient when using Granuflo is 41 meq/L.
>
> If you would like to change the bicarbonate or total buffer received by the patient, provide the nursing staff with an order for your desired bicarbonate or total buffer and the staff will adjust the setting.

Ex. 6, p. 4.

26. FMCNA's Chief Medical Office memorandum dated August 27, 2009, was addressed to FMS Medical Directors regarding the subject of "Concentrate Electrolyte Lookup Program – Version 2 with Expanded Bicarbonate Range." Ex. 7.

27. The August 27, 2009, memorandum provided, in part:

> The program is exactly the same as the first version that was distributed in July of 2009 with the exception of different bicarbonate selections:
>
> - The selectable bicarbonate range is now from 20 mEq/l to 40 mEq/l on the 2008K machine.
>
> - The selectable bicarbonate range is now from 25 mEq/l to 40 mEq/l on the 2008H machine.
>
> This program can be accessed by Medical Directors via DOCTORS CORNER and Attending physicians can have nursing staff access the program in the FMC4ME Intranet under Policies & Procedures > Clinical Services > Training Material > Concentrate Electrolyte Lookup Tool.

Ex. 7.

28. Ray Hakim, MD, former Chief Medical Officer for Fresenius Medical Services, authored a memorandum dated November 4, 2011 (the "Hakim Memo") that was addressed to all medical directors and attending physicians in FMS facilities regarding the subject of "Dialysate Bicarbonate, Alkalosis and Patient Safety." Ex. 8.

29. The Hakim Memo purported to discuss the results of a "case-control study" that "evaluated risk factors in HD patients who suffered from CP arrest in the facility (N=941 patients from 667 facilities) compared to other HD patients (N=80,516) within the same facilities between January 1 and December 31, 2010." Ex. 8, p. 4.

30. The Hakim Memo included graphs depicting the "Relative Risk of CP Arrest" based on patients' pre-dialysis serum bicarbonate levels and based on patients' pre-dialysis serum bicarbonate and serum potassium levels. Ex. 8, p. 4-5.

31. The "Conclusion" of the Hakim Memo provided as follows:

> Recent analysis performed using FMCNA hemodialysis (HD) patient safety data confirms that alkalosis is a significant risk factor associated with cardiopulmonary (CP) arrest in the dialysis unit, independent of and additive to the risk of CP arrest associated with pre-dialysis hypokalemia. The major cause of metabolic alkalosis

in dialysis patients is inappropriately high dialysate total buffer concentration. As recommended in previous communications, physicians should individualize dialysate bicarbonate and total buffer prescriptions. We further recommend that pre-dialysis serum bicarbonate level of > 24 mEq/L should prompt immediate review of dialysate bicarbonate prescription.

Ex. 8, p. 2.

32. The Hakim Memo reported several "findings," including the following:

- In September, 2011 the mean pre-dialysis bicarbonate level for FMCNA was 24.1 ± 3.4 mEq/L, with over 25% of patients at ≥26.0 mEq/L, 15% with ≥28.0 mEq/L and 3% with ≥30.0 mEq/L.

- Over time, the progressive shift towards higher ***pre-dialysis*** serum bicarbonate levels not only implies that more patients have alkalosis prior to dialysis, but that an even higher percentage of patients have alkalosis post-dialysis.

- The current analysis determined that: "*borderline elevated pre-dialysis bicarbonate levels and overt alkalosis are significantly associated with 6 to 8 fold greater risk of CP arrest and sudden cardiac death in the dialysis facility*".

- In light of these troubling findings, we strongly recommend that physicians adjust dialysate bicarbonate prescriptions monthly for individual patients, with immediate attention to patients with serum pre-dialysis bicarbonate level of > 24 mEq/L.

- The bicarbonate prescription entered into the dialysis machine underestimates the total buffer that the patient receives from the dialysate – *by ~8 mEq/L in the case of dialysate prepared from Granuflo (powder) or by ~4 mEq/L in the case of dialysate prepared from NaturaLyte (liquid)* – since acetate is rapidly converted into bicarbonate by the liver. Please familiarize yourself with the formulation utilized in each of your facilities and consider lower bicarbonate prescriptions (e.g. 31-33 mEq/L so that total buffer is no greater than 39-41 mEq/L when using Granuflo), and adjust monthly depending on each patient's pre-dialysis bicarbonate level.

Ex. 8, p. 2-3.

33. The Hakim Memo further provided, in part:

Pre-dialysis alkalosis and hypokalemia are modifiable risk factors associated with CP arrest….

> ….
>
> High pre-dialysis serum bicarbonate level was independent of and may potentiate the death risk associated with low pre-dialysis serum potassium. It is an actionable risk factor, by individualization of dialysate bicarbonate prescriptions to keep patients' pre-dialysis serum bicarbonate within a narrower range and to avoid alkalosis. We strongly recommend that physicians individualize dialysate prescriptions, review them monthly, with consideration of patient's pre-dialysis bicarbonate and dialysate total buffer….
>
> Many facilities have converted to the Fresenius powdered 'Granuflo' formulation that has total buffer equal to 'prescribed bicarbonate plus 8' – due to 4 mEq/L of sodium acetate in addition to the 4 mEq/L of acetic acid (acetate)….
>
> ….
>
> Previously, several memos were sent to you from the Medical Office to explain the difference in total buffer between NaturaLyte (liquid) and Granuflo (powder) dialysate formulations. The information was accompanied by a recommendation to address pre-dialysis alkalosis found in an increasing proportion of you patients, by decreasing the prescribed dialysate bicarbonate as needed. These previous memos, as well as a related article in the Medical Staff Newsletter, are accessible via Doctors Corner and also upon request….

Ex. 8, p. 5-6.

34. FMCNA maintains an intranet site, called Doctor's Corner, where all Chief Medical Office memoranda, including Exhibits 1-8 discussed above, are posted. Ex. 9, Nov. 16, 2014 Maddux Dep., 273:1-5; Ex. 10, Dec. 10, 2014 Maddux Dep., 747:5-11.

35. All attending physicians with privileges at FMCNA clinics and FMCNA medical directors, as well as many internal FMCNA staff, are granted access to Doctor's Corner. Ex. 9, Nov. 16, 2014 Maddux Dep., 273:1-15.

36. At his November 16, 2014, deposition, FMCNA's Chief Medical Officer Dr. Franklin Maddux testified, in part, that "many of our [FMCNA] physicians attend patients in our [FMCNA] facilities and attend patients in other facilities," and such physicians would have access to Doctor's Corner. Ex. 9, Nov. 16, 2014 Maddux Dep., 273:16-22.

37.

38.

39.

40.

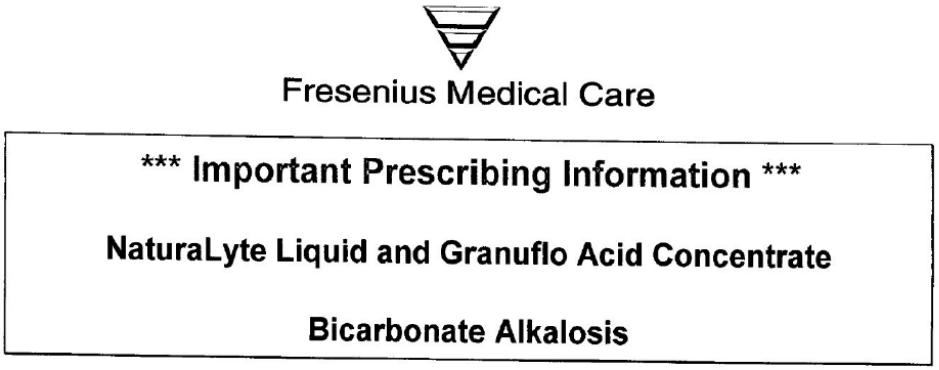
41.

42.

43.

44. On March 29, 2012, working with the FDA, FMCNA issued an "Important Prescribing Information" notification to all known customers that had purchased GranuFlo® or NaturaLyte®, whether it was a dialysis unit operated by FMCNA, DaVita, or anyone else. Ex. 14; Ex. 15, Nov. 19, 2014 Castle Dep., 623:22 - 624:14.

45. The March 29, 2012, notification was titled as follows:



Fresenius Medical Care

*** Important Prescribing Information ***

NaturaLyte Liquid and Granuflo Acid Concentrate

Bicarbonate Alkalosis

DATE: March 29, 2012

SUBJECT: Risk of Alkalosis with acetate containing dialysis acid concentrates

Ex. 14, p. 1.

46. The notification stated, in part:

> NaturaLyte Liquid contributes 4.0 mEq/L of acetate and Granuflo contributes 8.0 mEq/L of acetate to the final dialysate; which in addition to bicarbonate, combine

> to the total buffer that the patient receives from the dialysate. Acetate is also contained in the dialysis acid concentrates produced by other manufacturers. Since acetate is rapidly converted into bicarbonate by the liver, the bicarbonate prescription entered into the dialysis machine underestimates the total buffer that the patient receives from the dialysate by ~8 mEq/L with dialysate prepared from Granuflo (powder) or by ~4 mEq/L with dialysate prepared from NaturaLyte (liquid).

Id.

47. The notification also stated, in reference to the Hakim Memo, that "[r]ecent analysis performed using FMCNA hemodialysis (HD) patient safety data confirms that alkalosis is a significant risk factor associated with cardiopulmonary (CP) arrest in the dialysis unit …. A major cause of metabolic alkalosis in dialysis patients is inappropriately high dialysate total buffer concentration." Id.

48. The notification recommended that physicians individualize prescriptions and "review[] them monthly with consideration of patient's pre-dialysis bicarbonate and dialysate total buffer." Id. at 2.

49. At the February 6, 2017, pre-trial conference in Florella Dial v. Fresenius Medical Care Holdings, Inc., et al., D. Mass. Case No. 1:14-cv-11101, the plaintiff's counsel described the March 29, 2012, notification as follows:

> [I]t contains the essential causation, the link between alkalosis and the potassium, and it's an official notification where they're sending this out…. [I]t's information that if [a treating physician] had gotten earlier he might have changed what he did. But it's the essential causation story. It's saying that the alkalosis has these effects….

Ex. 16 (Tr. of Feb. 6, 2017 Pre-Trial Conference in Dial, at 66:5-14).

50.

51. On May 25, 2012, the FDA released a "Safety Communication" entitled "Dialysate Concentrates and Alkali Dosing Errors with Hemodialysis." Ex. 18. The communication discussed "acetate, acetic acid and/or citrate levels in dialysate concentrates and the need to consider the impact of these substances when ordering or administering the patient's dialysate prescription." It also noted that, "[w]hen metabolized, these potential sources of alkali can contribute to elevated bicarbonate levels in patients undergoing hemodialysis. This can contribute to metabolic alkalosis, which is a significant risk factor associated with cardiopulmonary arrest, low blood pressure, hypokalemia, hypoxemia, hypercapnia, and cardiac arrhythmia." Id.

52. Dr. David Goldfarb, one of Plaintiffs' nephrology experts, testified that nephrology fellows know from medical school that acetate metabolizes into bicarbonate in the liver. Ex. 19, June 19, 2015 Goldfarb Dep., 93:14 – 94:10.

53. Dr. Derek Fine, another of Plaintiffs' nephrology experts, testified that, before he ever was hired as an expert in this litigation, he knew about acetate and was teaching his nephrology fellows about acetate, how it can be metabolized to bicarbonate in the body, and to "look at the acetate" if a patient becomes alkalotic. Ex. 20, June 3, 2015 Fine Dep., 133:11 – 134:5.

54. Dr. Paul Miller, who instigated the 2012 labeling recall and litigation against Fresenius regarding GranuFlo®, agreed that "most nephrologists who have been through high school and then college and then medical school, would understand that acetate converts in the body to bicarbonate." Ex. 21, June 24, 2015 Miller Dep., 113:16-25.

55. At his deposition on June 19, 2015, Dr. Goldfarb further testified, in part:

Q. You know that the labels for GranuFlo show the acetate concentration, right?

A. Yes.

Q. And the labels for NaturaLyte contain its acetate concentration, correct?

….

A. I assume that's true, yes.

….

Q. And you teach your nephrology fellows that they should read the labels on drugs that they prescribe their patients, correct?

A. To drugs, dialysate, of course.

Q. Acid concentrates?

A. Yes.

Ex. 19, Goldfarb Dep., 155:18 – 156:7

56. At his deposition on June 2, 2015, Dr. Steven Borkan, another of Plaintiffs' nephrology experts, testified, in part:

Q. And prior to being retained in this case, did you have the ability to determine what the components were that were in NaturaLyte?

A. Yes, I did. If I were to have looked at the ingredients on the floor, like most nephrologists, I could have bent over and read the labels.

Ex. 22, June 2, 2015 Borkan Dep., 11:24 - 12:6

57. At his deposition on June 3, 2015, Dr. Fine testified that NaturaLyte® is used in his dialysis unit in different formulations, and both the "jugs" and "barrels" of NaturaLyte® contain labels that identify the contents in the acid concentrate, including the acetate concentration. Ex. 20, Fine Dep., 135:9 - 139:19, 142:9-13.

58. At his deposition on June 3, 2015, Dr. Fine also testified, in part:

Q. What type of hemodialysis machines do you use in the inpatient clinic?

A. We use the Fresenius. There's a 2008K. There's one that's a KT or some – little bit different, one you can do it, it's got a touch screen and the other one you actually have to adjust using buttons below the screen. I've been told that they do the same thing.

Q. Okay. And what about at the clinic, what hemodialysis machines do you use at outpatient clinic?

A. Same.

Q. Same okay. So are you aware that there's a screen on the hemodialysis machine that shows, for example, the bicarbonate prescription?

A. Yes.

Q. And are you aware that the screen can also show various electrolytes, including the acetate?

A. Yes.

Ex. 20, Fine Dep., 134:15 – 135:8

59. At his deposition on June 19, 2015, Dr. Goldfarb further testified, in part:

Q. Are you aware of what is and can be displayed on the screens of the Fresenius hemodialysis machines?

A. Of course I've seen in some of the documents pictures of the screens, yes.

Q. So you're aware that it shows, for instance, the bicarbonate prescription that's being delivered to the patient, correct?

A. The bicarbonate prescription, right.

Q. And you're also aware that it displayed the acetate content of the dialysate?

A. I did see that.

Ex. 19, Goldfarb Dep., 129:21 – 130:8.

60.

Facts Applicable to Plaintiff Boyd

61.

62.

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74.

Facts Applicable to Plaintiff Carter

75.

76.

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79.

80.

Facts Applicable to Plaintiff Clark (Decedent Jenkins)

81.

82.

83.

84.

Facts Applicable to Plaintiff Dennis

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86.

87.

88.

Facts Applicable to Plaintiff Dillingham

89.

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91.

92.

Facts Applicable to Plaintiff Dunaway (Decedent Cothern)

93.

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96.

Facts Applicable to Plaintiff McGhee

97.

98.

99.

100.

Facts Applicable to Plaintiff McNulty

101.

102.

103.

104.

105.

Facts Applicable to Plaintiff Randall

106.

107.

108.

109.

Facts Applicable to Plaintiff Ross

110.

111.

112.

113.

Facts Applicable to Plaintiff Walker (Decedent Myles)

114.

115.

116.

117.

118.

119.

Facts Applicable to Plaintiff Williams (Decedent Hughes)

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121.

122.

123.

124.

125.

126.

Facts Applicable to Plaintiff Jerry

127.

128.

129.

130.

131.

Facts Applicable to Plaintiff Kazos

132.

133.

134.

135.

136.

137.

138.

139.

140.

Facts Applicable to Plaintiff Riben

141.

142.

143.

Facts Applicable to Plaintiff Cameron

144.

145.

146.

Dated: September 8, 2017

Respectfully submitted,

/s/ James F. Bennett
James F. Bennett
Megan S. Heinsz
DOWD BENNETT LLP
773 Forsyth Blvd., Suite 1900
St. Louis, MO 63105
(314) 889-7300
(314) 889-7302 (fax)
jbennett@dowdbennett.com
mheinsz@dowdbennett.com

William H. Kettlewell (BBO # 270320)
Maria R. Durant (BBO # 558906)
Sara E. Silva (BBO # 645293)
COLLORA LLP
100 High Street, 20th Floor
Boston, MA 02110
(617) 371-1000
(617) 371-1037 (fax)
wkettlewell@collorallp.com
mdurant@collorallp.com
ssilva@collorallp.com

Leigh Anne Hodge
BRADLEY ARANT BOULT CUMMINGS LLP
One Federal Place
1819 Fifth Avenue North
Birmingham, AL 35203
(205) 521-8000
(205) 521-8800 (fax)
lhodge@babc.com

Juanita Brooks
FISH & RICHARDSON
12390 El Camino Real
San Diego, CA 92130
(858) 678-5070
(858) 678-5099 (fax)
brooks@fr.com

Counsel for FMCNA

CERTIFICATION OF SERVICE

I hereby certify that a true and correct copy of the foregoing document was served on Plaintiffs' counsel by e-mail on September 8, 2017, to:

mollyb@hbsslaw.com

matt@sill-law.com

dunbarwatt@gmail.com

/s/ James F. Bennett